AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph at page 3, line 22 to page 4, line 7 with the following paragraph:

The carrier used in this invention is biocompatible in that it is not toxic and does not elicit severe inflammatory reactions in the body. The carrier is also bioresorbable in that it can be at least partially, and preferably entirely, resorbed at the repaired locus within a clinically acceptable period of time, e.g., 4 months to a year. The carrier can include a matrix or "scaffold" structure, or it can be substantially matrix-free. The carrier may be solid (e.g., porous or particulate), or in a gel, paste, liquid or other injectable form. Suitable carriers contain materials that include, but are not limited to, allogenic tissue (e.g., devitalized allogenic, autologous, or xenogenic cartilage tissue), collagen (e.g., Types I and II collagen), celluloses (e.g., alkylcelluloses such as carboxymethylcellulose), calcium phosphates (e.g., hydroxyapatite), poloxamers (e.g., ~~PLURONIC F127~~PLURONIC F127®), gelatins, polyethylene glycols (e.g., PEG 3350), dextrins,

vegetable oils (e.g., sesame oil), and polymers comprised of lactic acid, butyric acid, and/or glycolic acid. Autologous or autogenic blood can also be included in the carrier, because it has been found that such inclusion speeds up the healing process.

Please replace the paragraph at page 21, lines 3-12 with the following paragraph:

In yet another embodiment of the present invention, the osteogenic device is prepared immediately prior to its delivery to the defect locus. For example, carboxymethylcellulose (CMC) containing devices can be prepared on-site, suitable for admixing immediately prior to surgery. In one embodiment, low viscosity CMC (~~AQUALON~~AQUALON®) is packaged and irradiated separately from the osteogenic protein OP-1. The OP-1 protein then is admixed with the CMC carrier, and tested for osteogenic activity. Devices prepared in this manner are as biologically active as the conventional device without CMC. The devices repair defect loci by inducing cartilage or tissue formation. The amount of osteogenic protein effective for this purpose can be readily determined by one skilled in the art.

Please replace the paragraph at page 32, lines 2-14 with the following paragraph:

This example describes another study on the efficacy of osteogenic protein in regenerating new tissue at a defect site. This study contained five experimental groups that were divided into two sub-studies. Groups I-III compared the effects of different OP-1 carriers on the repair of identical thyroid cartilage defects. The tested carriers were CMC, CMC/blood paste, and HELISTAT® sponge (a Type I collagen composition). Groups IV and V addressed different animal models and surgical methods, where larger defects as used in human clinical practice were created and repaired by combinations of OP-1/CMC device, ~~VICRYL~~VICRYL™ surgical mesh, and ~~PYROST~~PYROST® (a bone mineral composition) rigid supports. These latter two groups were approximations of the combined product and procedure envisioned for a clinical setting. Surgeries on Groups I - III were performed one or two months before surgeries on Groups IV and V. The experimental protocol is summarized below in Table II.

Please replace Table II at page 33, lines 1-22 with the following table:

TABLE II: Dog Larynx Reconstruction Using OP-1

Group	Dogs	Defect	OP-1	Duration
I	3	I	A	4 months
II	3	I	B	4 months
III	3	I	C	4 months
IV	3	II	A	6 months
V	3	III	A x 2	6 months

Defect

I: Partial removal of right thyroid lamina. OP-1 was applied to the defect and contained between perichondrial layers adjacent to the thyroid cartilage.

II: Partial vertical laryngoctomy. An OP-1/CMC device was implanted between layers of ~~VICRYL~~VICRYL™ mesh. The implant was fixed to ~~PYROST~~PYROST® rods, which positioned and shaped the implant. The implant was contained between a pharyngeal mucosa flap (inside) and the perichondrium (outside).

III: Extended partial vertical laryngoctomy. OP-1/CMC devices (2 per animal) were implanted and fixed as described for partial vertical laryngoctomy.

OP-1

A. OP-1/CMC device. B. OP-1 in CMC/blood paste. C. OP-1 applied to HELISTAT®

Please replace the paragraph at page 38, lines 15-21 with the following paragraph:

In this study, three different osteogenic devices were used to deliver OP-1. They were the OP-1/CMC device, OP-1/CMC/blood paste, and ~~OP-1/HELISTAT~~OP-1/HELISTAT® sponge. The blood paste device was prepared by mixing 160 μl OP-1 at 5mg/ml with 400 μl 20% CMC via a syringe connection, followed by addition of 240 μl freshly drawn autologous blood and continuous mixing. The final volume applied to the defect was 0.8 ml. The ~~HELISTAT~~HELISTAT® device was prepared by applying 225 μl OP-1 onto 6 mg ~~HELISTAT~~HELISTAT® sponge for every 2 cm^2 defect area.

Please replace the paragraph at page 38, line 22 to page 39, line 1 with the following paragraph:

Three different treatment methods were studied. In the first treatment method, defects in the left thyroid cartilage lamina were created as described above; OP-1 devices were applied to the defect areas and maintained between perichondrial layers adjacent to the defect. In the second treatment method, partial vertical laryngoctomy was initially performed, and the ~~OP-1/HELISTAT~~OP-1/HELISTAT® device was implanted; immobilization of

the reconstructed area was achieved with ~~PYROST~~PYROST® as described in Example 6; the implant was placed between a pharyngeal mucosal flap (inside) and the perichondrium (outside). The third treatment method involved anterior cricoid split and luminal augmentation; in this method, the ~~OP-1/HELISTAT~~OP-1/HELISTAT® device was implanted and immobilized with PYROST®.

Please replace the paragraph at page 41, lines 4-12 with the following paragraph:

Group III: ~~OP-1/HELISTAT~~OP-1/HELISTAT®

This group of animals were treated with the first treatment method, *supra*, using the ~~OP-1/HELISTAT~~OP-1/HELISTAT® sponge device. The defects in all dogs healed completely by the formation of new bone. Unlike the Group I and II dogs, the Group III dogs contained less ligament-like tissue at the healed defect sites. In one animal, the new tissue was nicely positioned within the margins and only a small amount protruded laterally. In other animals, the new tissue formed multiple layers; in one

dog the new tissue was completely out of the defect frame, inducing bone formation in the adjacent area.

Please replace the paragraph at page 41, lines 13-22 with the following paragraph:

The abundance of ossification was determined by the size and positioning of the ~~HELISTAT~~HELISTAT® sponge. Margins of the new bone and the old cartilage were separated by a thin fibrous layer. Small amounts of collagen from the ~~HELISTAT~~HELISTAT® sponge remained unresorbed. Dislocation of the sponge in one animal led to abundant bone formation outside the defect site. The orientation of bone trabeculi followed the path of collagen fibers within the sponge, suggesting that the ossification was guided by the carrier matrix to which the morphogen had been bound. The decrease in the amount of ligament-like tissue observed in this group of animals was likely due to the lesser ability of Type I collagen to attract ligament precursor cells.

Please replace the paragraph at page 41, line 24 to page 42, line 3 with the following paragraph:

This group of animals were treated with the second treatment method, *supra*, using the ~~OP-1/HELISTAT~~OP-1/HELISTAT® sponge device. The anterior half of the left thyroid lamina and the surrounding soft tissues (ventricular and vocal folds) were surgically removed. Immobilization of the reconstructed area was performed with ~~PYROST~~PYROST®. The implant was placed between a pharyngeal mucosal flap (inside) and the perichondriurn (outside). Regeneration of the larynx skeleton was still in progress with bone filling in the removed thyroid cartilage, as of 4 months post-operation. The new bone was still undergoing remodeling and provided a good scaffold for the larynx skeleton integrity. The gap between the vocal and thyroid cartilages was filled with unorganized connective tissue, allowing normal air flow.

Please replace the paragraph at page 42, lines 5-16 with the following paragraph:

This group of animals were treated with the third treatment method, *supra*, using the ~~OP-1/HELISTAT~~OP-1/HELISTAT® sponge device. The anterior part of the cricoid arcus was transected and a lumen extension was created by external implantation of ~~PYROST~~PYROST®. The space between the cricoid ends was filled with the ~~OP-1/HELISTAT~~OP-1/HELISTAT® device. The lumen remained extended while the ~~PYROST~~PYROST® was partially removed or powdered and integrated with the new bone. The central area was occupied by new bone that was undergoing active remodeling. Surprisingly, minimal bone tissue was formed adjacent to the ~~PYROST~~PYROST®, which might have served as an affinity matrix for the OP-1 protein released from the adjacent ~~HELISTAT~~HELISTAT® sponge. In one specimen, the new bone and ~~PYROST~~PYROST®-surrounded bone formed an extended bone area that did not compromise the lumen diameter. No ligament-like tissue was formed, indicating the lack of precursor cells in the vicinity of the cricoid cartilage.